

**REMARKS**

Claims 1-13 and 15-43 were pending in the application. Claims 1 and 18-43 have been canceled, without prejudice, as being directed to a non-elected invention. Claims 5-8 and 17 have been amended and new claims 44-48 have been added. Accordingly, upon entry of this amendment, claims 2-13, 15, 16, 17 and 44-48 will remain pending. For the Examiner's convenience the currently pending claims are set forth in Appendix A.

Applicants submit herewith a "Version with Markings to Show Changes Made," which indicates the specific amendments made to the claims. *No new matter has been added.*

Support for the amendments to the claims and for new claims 34-36 may be found throughout the specification and claims as originally filed.

Any amendments to and/or cancellation of the claims was done solely for the purpose of expediting prosecution of the present application. Applicants reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

***Response to Restriction Requirement***

The Examiner has required restriction to one of the following inventions under 35 U.S.C. §121:

- I. Claim 1, drawn to nucleic acid;
- II. Claims 2-7 and 17, drawn to polypeptide;
- III. Claims 8-16, drawn to a fusion polypeptide;
- IV. Claims 18-19, drawn to method of making polypeptide of Group II;
- V. Claim 20, drawn to method of making protein of Group III;
- VI. Claims 21-37, drawn to method of identifying an ACE-2 therapeutic;
- VII. Claim 38, drawn to method of modulating ACE-2 activity;
- VIII. Claims 39-41, drawn to methods of treating and preventing blood pressure or disease or disorder;
- IX. Claim 42, drawn to method of determining risk of developing a disease or condition caused by aberrant ACE-2 activity; and
- X. Claim 43, drawn to method of identifying ACE-2 polypeptide substrate.

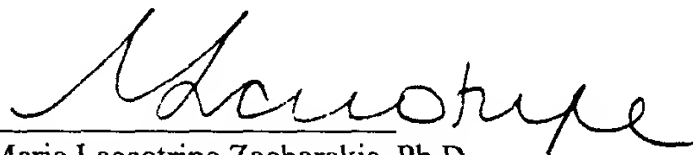
Applicants hereby elect the Group II invention (claims 2-7 and 17, drawn to polypeptides) for prosecution in this application, *with traverse*. Applicants respectfully request that the Examiner re-group and examine Groups II and III, on the grounds that these groups are ***both directed to polypeptides***. Contrary to the Examiner's assertion, claims 8-16 are not directed to fusion polypeptides, but to polypeptides that are fragments or variants of the polypeptides grouped by the Examiner in Group II. As such, the searches with regard to these inventions would be co-extensive and would not involve a burden on the Examiner. Applicants, therefore, request that the examiner examines Groups II and III.

Applicants reserve the right to traverse the restriction between the non-elected groups in this or a separate application.

#### SUMMARY

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



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Limited Recognition Under 37 C.F.R. §10.9(b)

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Claims 5-8 and 17 were amended as follows:

5. **(Amended)** The An isolated polypeptide ~~of claim 4, which is~~ encoded by the nucleic acid having ATCC Designation No. 209510.

6. **(Amended)** The An isolated polypeptide ~~of claim 4, which is~~ encoded by a nucleic acid ~~having~~ comprising the nucleotide sequence set forth in SEQ ID NO:1.

7. **(Amended)** The An isolated polypeptide ~~of claim 6, which has~~ comprising the amino acid sequence set forth in SEQ ID NO:2.

8. **(Amended)** An isolated polypeptide comprising an amino acid sequence which is at least about 90% identical to ~~at least about 15 consecutive amino acid residues of~~ the amino acid sequence set forth in SEQ ID NO:2.

17. **(Amended)** An isolated polypeptide comprising ~~an amino acid sequence which is at least about 70% similar to~~ at least about 50 consecutive amino acid residues of SEQ ID NO:2 and which has a bioactivity of an ACE-2 polypeptide.

**APPENDIX A**

2. An isolated polypeptide comprising an amino acid sequence having an amino acid identity of at least about 70% with the entire amino acid sequence set forth in SEQ ID NO:2.
3. The isolated polypeptide of claim 2, which is a mammalian polypeptide.
4. The isolated polypeptide of claim 3, wherein the polypeptide is a human polypeptide.
5. An isolated polypeptide encoded by the nucleic acid having ATCC Designation No. 209510.
6. An isolated polypeptide encoded by a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:1.
7. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.
8. An isolated polypeptide comprising an amino acid sequence which is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO:2.
9. The isolated polypeptide of claim 8, which has a bioactivity of an ACE-2 polypeptide.
10. The isolated polypeptide of claim 9, which binds a target peptide.
11. The isolated polypeptide of claim 10, which binds angiotensin I.
12. The isolated polypeptide of claim 11, which hydrolyzes angiotensin I into angiotensin (1-9).
13. The isolated polypeptide of claim 10, which binds kinetensin.
15. The isolated polypeptide of claim 13, which hydrolyzes kinetensin into kinetensin (1-8).

16. The isolated polypeptide of claim 8, which is encoded by a nucleic acid which hybridizes to a nucleic acid having the nucleotide sequence set forth in SEQ ID NO:1 or complement thereof.

17. An isolated polypeptide comprising at least about 50 consecutive amino acid residues of SEQ ID NO:2 and which has a bioactivity of an ACE-2 polypeptide.

44. An isolated polypeptide comprising at least about 50 consecutive amino acid residues of SEQ ID NO:2.

45. An isolated polypeptide consisting of the amino acid sequence set forth in SEQ ID NO:2.

46. An isolated naturally occurring allelic variant of a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2.

47. An isolated polypeptide comprising an amino acid sequence which is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO:2, wherein said polypeptide has a bioactivity of an ACE-2 polypeptide.

48. The polypeptide of any one of claims 5, 6, 7, 8, 17, 44, 45, 46 or 47, further comprising heterologous amino acid sequences.